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Evaluating the efficacy of different tribendimidine combinations against intestinal worms (soil-transmitted helminths)

Submission date
07/07/2016

Recruitment status
No longer recruiting

Registration date
19/07/2016

Overall study status
Completed

Last Edited
30/08/2023

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Soil-transmitted helminthes, such as hookworm and whipworm (intestinal worms that are spread via contaminated soil) are a serious health concern in South-East Asia, Africa and South America, especially in school-age children. The standard treatment, recommended by the World Health Organization (WHO), is use of preventive chemotherapy drugs albendazole and mebendazole. However, overuse of these drugs increases the chance that the worms will become resistant to their effects. To be prepared for this situation new drugs have to be identified to replace the old ones. Tribendimidine (a general anti-worms drug) has been shown to be effective in the treatment of soil-transmitted helminthes (STH) and could act as albendazole/mebendazole replacement in case of resistance. Additionally, none of the current drugs used to treat STH are particularly effective against whipworm, except the new drug oxantel pamoate. The aim of this study is to investigate the most effective combination of albendazole plus oxantel pamaote for the treatment of STH infections.

Who can participate?
Patients aged between 15 and 18 years old with hookworm eggs in their stool, who are otherwise healthy.

What does the study involve?
Participants are randomly allocated to one of four groups who receive a single dose of medication on day one of the study. Those in the first group receive a dose of tribendimidine (400mg) plus oxantel pamoate (25mg/kg); those in the second group receive a dose of tribendimidine (400mg) plus ivermectin (200µg/kg); those in the third group receive a dose of tribendimidine (400mg) plus placebo (dummy pill); and those in the fourth groups receive a dose of albendazole (400mg) plus oxantel pamoate (25mg/kg). At the start of the study and then after 14-21 days, participants provide stool samples on two consecutive days so that the amount of STH eggs can be counted to find out the efficacy of the medications.

What are the possible benefits and risks of participating?
All participants enrolled in the study will benefit from a treatment against STHs. Very few

negative side effects have been reported for the medications used in this study, however there is a small risk of abdominal (tummy) cramps, fever, nausea and headache, and vertigo (spinning sensation).

Where is the study run from?
1. Public Health Laboratory Ivo de Carneri (Tanzania)
2. Centre Suisse de Recherches Scientifiques en Côte d'Ivoire (Côte d'Ivoire)

When is the study starting and how long is it expected to run for?
February 2015 to May 2017

Who is funding the study?
Swiss National Science Foundation (Switzerland)

Who is the main contact?
Professor Jennifer Keiser
jennifer.keiser@unibas.ch

Contact information

Type(s)
Scientific

Contact name
Prof Jennifer Keiser

Contact details
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Additional identifiers

Study information

Scientific Title
Efficacy and safety of tribendimidine plus oxantel, tribendimidine plus ivermectin, albendazole plus oxantel pamoate and tribendimidine alone against hookworm and concomitant soil-transmitted helminth infections: a randomised controlled multi-country trial

Acronym
Tricombi

Study objectives
The aim of this study is to provide evidence that tribendimidine in combination with oxantel pamoate or ivermectin could serve as an alternative to the currently most efficacious combination albendazole-oxantel against soil-transmitted helminth infections in Côte d’Ivoire and Tanzania.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Ethikkommission Nordwest-und Zentralschweiz EKNZ, 25/06/2015, ref: EKNZ UBE 15/35 (Switzerland)
2. Zanzibar Medical Research and Ethics Committee ZAMREC, 11/07/2016, ref: ZAMREC /0001 /July/016 (Tanzania)
3. Comité National d'Ethique pour la Recherche CNER, 09/09/2016, ref : 083/MSHP/CNER-kp

Primary study design
Interventional

Study design
Single-blinded randomized interventional study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Hookworm infection

Interventions
Study participants eligible for treatment will be randomly assigned to one of the four treatment arms using a computer-generated stratified block randomization code. The random allocation sequence with varying random blocks of four or eight will be provided by a statistician.

Group 1: One single dose of tribendimidine (400mg) plus oxantel pamoate (25mg/kg)
Group 2: One single dose of tribendimidine (400mg) plus ivermectin (200µg/kg)
Group 3: One single dose of tribendimidine (400mg) plus placebo
Group 4: One single dose of albendazole (400mg) plus oxantel pamoate (25mg/kg)

At follow-up (after 14-21 days) participants will be asked to provide a second time two stool samples on two consecutive days.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
1. Tribendimidine 2. Oxantel pamoate 3. Ivermectin 4. Albendazole

Primary outcome(s)
Egg-reduction rates against hookworm are measured calculating the mean reduction in egg-counts at follow-up (after 14-21 days) compared to baseline (based on quadruplicated Kato-Katz thick smears).

Key secondary outcome(s)

1. Cure rate (CR) against hookworm is the percentage of children egg negative calculated at follow-up (14-21 days post treatment) based on a quadruplicated Kato-Katz thick smear
2. Cure rate (CR) and egg-reduction rate (ERR) against A. lumbricoides and T. trichiura are egg free children at follow-up (14-21 days post treatment based on a quadruplicated Kato-Katz thick smear) or the mean reduction in egg-counts at follow-up (after 14-21 days) compared to baseline (based on quadruplicated Kato-Katz thick smear)
3. Pharmacokinetic parameters are determined based on concentration of the different drugs measured
4. Safety is measured based on number of children reporting adverse events at the time points 3 and 24 hours post treatment using a standardized questionnaire

Completion date
01/05/2017

Eligibility

Key inclusion criteria
1. Written informed consent signed by parents and/or legal guardian; and assent by children
2. Able and willing to be examined by a study physician at the beginning of the study
3. Able and willing to provide two stool samples at the beginning (baseline) and approximately three weeks after treatment (follow-up)
4. Positive for hookworm eggs in the stool
5. Absence of major systemic illnesses (e.g. diabetes, anemia) as assessed by a medical doctor, upon initial clinical assessment
6. No known or reported history of chronical illness as cancer, diabetes, chronic heart, liver or renal disease
7. No recent anthelminthic treatment (within past 4 weeks)
8. No known allergy to study medications (e.g. albendazole, mebendazole)
9. Aged 15-18 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Key exclusion criteria
1. No written informed consent by parents and/or legal guardian and assent for children
2. Presence of major systemic illnesses (e.g. diabetes, anemia) as assessed by a medical doctor, upon initial clinical assessment
3. History of acute or severe chronic disease
4. Recent use of anthelminthic drug (within past 4 weeks)
5. Attending other clinical trials during the study
6. Negative diagnostic result for hookworm eggs in the stool

Date of first enrolment
25/07/2016

Date of final enrolment
02/12/2016

Locations

Countries of recruitment
Côte d'Ivoire

Tanzania

Study participating centre
Public Health Laboratory Ivo de Carneri
Tanzania
-

Study participating centre
Centre Suisse de Recherches Scientifiques en Côte d'Ivoire
Côte d'Ivoire
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Sponsor information

Organisation
Swiss Tropical and Public Health Institute

ROR
https://ror.org/03adhka07

Funder(s)

Funder type
Research organisation

Funder Name
Swiss National Science Foundation

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/11/2017		Yes	No
Other publications	diagnostic comparison conducted in the framework of the clinical trial based exclusively on samples collected in Tanzania	04/06/2018	30/08/2023	Yes	No